RM
859
R313
v.6
no.4
c.1
GERSTS

RADIUM

EDITED BY
CHARLES H. VIOL, Ph. D.
AND
WILLIAM H. CAMERON, M. D.

VOL. VI JANUARY, 1916 No. 4

CONTENTS

Radium in the Treatment of Carcinomas of the Cervix Uteri and Vagina, Howard A. Kelly, M. D. and Curtis F. Burnam, M. D. 73

Reviews and Abstracts 83

Contribution on the Therapeutic Value of the Intravenous Injection of Soluble Radium Salts in the Treatment of Pernicious Anaemia and Leukaemia, Frederick Proescher, M. D., and B. R. Almquest, M. D. 85

LIBRARY
NOV 13 2001
UNIVERSITY OF TORONTO

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

THE PROPERTY OF
ACADEMY OF MEDICINE,
TORONTO.
13 QUEEN'S PARK

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D., and William H. Cameron, M. D. with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

Subscription $2.50 per year, or 25 cents per copy in the United States and Canada in all other countries $3.75 per year.

Address all communications to the Editors, Forbes and Meyran Avenues, Pittsburgh, Pa.

VOL. VI. JANUARY, 1916 No. 4

RADIUM IN THE TREATMENT OF CARCINOMAS OF THE CERVIX UTERI AND VAGINA*

HOWARD A. KELLY, M.D. AND CURTIS F. BURNAM, M.D.
BALTIMORE.

The scope of this paper has been intentionally limited to a consideration of the value of radium in treating the malignant epithelial new growths of the vagina and cervix uteri. Equally interesting technical problems and clinical phenomena are met when radium is used in treating other kinds of malignant tumors, for example, the sarcomas and carcinomas, and tumors in other organs, as the bladder, breast, tongue, etc. The technic, the indications for treatment and results obtained vary with the type of tumor and its location so greatly that each demands separate consideration. It is especially difficult to have to exclude the adenocarcinoma of the fundus uteri, as it is quite radiosensitive and as we have of it the most excellent material, both clinical and anatomic. The problems connected with its surgical as well as radium treatment, however, differ widely from those of the cervical—uterine and vaginal—cancers.

Absolute valuation of a therapeutic agent is obtainable only after all methods of using it have been tried out on carefully selected and classified cases over a period of years. Our knowledge of the curative action of radium on cancers of the uterine cervix and vagina is as yet in its infancy; nevertheless, its ultimate possibilities, viewed in the light of present experience, seem very great. That it does greatly increase the percentage of the curable cases of these cancers and correspondingly diminishes the percentage of the incurable is already evident and demonstrable.

So far as is known, untreated cancers of the cervix uteri and vagina

*Journal Am. Med. Assn. vol. 65, pp. 1874-8, Nov. 27, 1915. Read before the Section on Obstetrics, Gynecology and Abdominal Surgery at the Sixty-Sixth Annual Session of the American Medical Association, San Francisco, June, 1915.

1. Wertheim: Strahlentherap., iii, 537.
2. Kronig: Strahlentherap., iii, 28.

do not heal spontaneously and do inevitably lead to painful death after a period of suffering varying from a few months to several years.

The continuous and painstaking work and investigations of many surgeons and pathologists through a period of more than two decades have firmly established the accepted surgical technics with their proved five year cures. During this time there has been accumulated an immense store of information regarding the occurrence, the etiologic importance of trauma, the histopathology, the avenues of extension, the rate of growth and the complications of these malignant, epithelial new growths.

The Wertheim radical hysterectomy, in our opinion, yields a higher percentage of permanent cure in cancer of the uterine cervix than does any other operative procedure. It affords, however, much less help in the treatment of primary cancer of the vagina.

Nothing is more misleading than a gross statistical statement of so many patients operated on, such a primary mortality and so many permanent cures. The operator who takes only the early and moderately advanced cases has a lower primary mortality and a higher permanent cure rate than does the one who treats many of the border-line operable type. Where a professional and public educational campaign against the disease has been carried out, as in Vienna, the proportion of easily operable cases is much larger than where such advanced methods have not been followed. Great need exists for reports on carefully classified groups of cases, and not only the extent of the growth but also its histologic type should be taken into account in the group separations.

A statistical report by Howard A. Kelly and J. Craig Neel of the cases of uterine cervix cancer seen at the Johns Hopkins Hospital up to August, 1913, shows 57 per cent. operable, 11 per cent, primary mortality and 25 per cent. permanent cure. It is of interest that only one case of adenocarcinoma remained free from recurrence for two years after the operation. Wertheim[1] states that 50 per cent. of the cases are operable, and that 50 per cent. of those patients operated on remain well. Kroenig[2] states that not more than 20 per cent. of the cervix cancers are permanently cured by operation and less than 5 per cent. of the primary vaginal cancers.

The present report is based on a series of 213 cases of cancer of the uterine cervix and vagina treated with radium at the Howard A. Kelly Hospital, between Jan. 1, 1909, and Jan. 1, 1915. Although one of the cures dates from 1909, it was not until December, 1912, that we secured sufficient radium and developed sufficient enthusiasm to employ it systematically, and indeed only in the last eighteen months have the patients in the operable class been invariably radiated as well as operated on. Of the 213 cases, fourteen were operable and 199 inoperable or inoperable recurrent cancers. We have refused treatment to no inoperable case that has come to the hospital, although we have discouraged the coming of patients with evident general carcinomatosis. Before passing to a detailed analysis of these cases and the results obtained by treatment, it seems necessary to discuss very briefly some questions of technic, of histologic change (in radiated tissue) and of theory as to the mechanism of the action of the rays on tissues both normal and pathologic.

It would be most profitable here to digress into a most fascinating field of human knowledge, but time does not permit even a bare outlining of the physical properties of radium. Suffice it to say that radium is obtainable in stable form as a bromid, chlorid or sulphate, and that by appropriate means radium emanation, a gas, can be separated from the radium salts.

In order to carry out such a radium radiation, as the cases under consideration require, it is necessary to have applicators which hold either dry radium salts or the emanation of radium. The emanation has a great advantage in that it is possible to vary the size, shape and strength of the applicator at will and for each case; it requires, however, considerable skill in glass blowing and in mercury vacuum-pump manipulation.

Figure 1 shows a few applicators; the millimeter rule permits an easy estimation of size. The small tube between the needles is a glass capillary in which any amount of emanation between a fraction of a millicurie and a curie (equal to a gram of radium) can be placed. This can be inclosed in a metal container of its own shape and length, or it may be placed in the outer end of one of the record syringe hypodermic needles, shown on either side of it. Immediately to the right of the needle is an applicator containing 100 mg. of pure radium chlorid in a glass tube encased in a thin platinum envelope 0.4 mm. thick, and all covered by a small rubber cot about 3 mm. thick. Still further to the right is shown the platinum envelope necessary to hold 100 mg. of pure radium chlorid. The last figure to the right shows a small flat applicator. These can readily be made an inch or two in diameter, and will hold immense or small amounts of emanation as desired. Through the glass container are emitted from the radium two kinds of rays: the beta and the gamma.

The beta ray is particulate matter, a negatively charged ion, deflectable by an electromagnet, entirely absorbed by 3 mm. of lead, or 2 cm. of tissue. Occurring in ten times the quantity of the gamma rays, it produces much more marked destructive biologic effects.

The gamma ray is a vibration of ether of extremely short wave length. It is comparable to ordinary light and the Roentgen ray. It is extremely penetrating, passing through inches of lead or feet of tissue.

When tested by the heavy metals, such as lead, platinum, etc.. both the beta and the gamma rays vary as to penetration. There are soft, medium and hard rays of each class; however, according to Keetman and Mayer, the absorption of these rays in tissue is as if they were uniform, that is, for a given thickness of tissue there is an equal per-

Thickness of Tissue Traversed, cm.	Absorption of Tissue, per Cent.	Radiation Transmitted per Cent.	Dispersion Correction	Intensity of Radiation per sq. mm.	Amount of Radium Unit to Give 1 mg.
0	0	100	0	1	2,500
1	5	95	0.695	0.66	3,788
2	9.75	90.25	0.51	0.464	5,410
3	14.3	85.7	0.39	0.335	7,465
4	18.6	81.4	0.31	0.251	9,950
5	22.17	77.83	0.25	0.194	12,880
6	26.06	73.94	0.207	0.153	16,310
7	29.76	70.24	0.174	0.122	20,480
8	33.3	66.7	0.147	0.098	25,500
9	36.7	63.3	0.128	0.081	30,850
10	40	60	0.11	0.066	37,500

centage of absorption of the rays going through it. The work of Keetman and Mayer carried out with mesothorium is being repeated with radium in our physical laboratory, but is not yet finished. According to them, 8 per cent. of the beta rays are absorbed by each one-tenth millimeter of tissue and 5 per cent. of the gamma rays by each centimeter of tissue. Beta and gamma rays can be used together or the gamma ray can be used alone by placing a 2 mm. lead screen or a 1 mm. platinum screen between the radium and the part treated..

In addition to absorption in tissue, another most important factor in determining the intensity of radiation, on any surface, from a uniform source, is the distance from the source; for the intensity as in all spherical dispersion varies inversely with the square of the distance.. If, for example, we place 1 mg. of radium 1 mm. distant from a 1 mm. square surface and then extend the distance to an inch or 25 mm., the intensity at 1 mm. distance is 625 times that at the distance of 1 inch, as can be readily calculated.

Taking the 1 mg. at 1 mm. in one second on 1 square mm. of surface, as the unit of dosage, and taking in the factors of sperical dispersion and tissue absorption, the table inserted above shows the effects at various depths and the quantity of radium which is necessary to produce a unit dose in one second when the applicator is placed 5 cm. away from the surface.

A factor not considered in the table but of the highest importance, is that, within certain limits, increasing the duration of the application correspondingly diminishes the amount of radium required to produce the unit energy: for example, a unit dose at a depth of 5 cm. can be secured with 1 gm.radium in 12.88 seconds, or with 200 mg. of radium in a little more than a minute.

Figure 2 shows graphically the changes in intensity of gamma radiation at different depths in the tissue.

It is evident that when beta radiation is needed in the depths, it can be secured by placing the emanation-containing needles at equal distances, never greater than 1 cm. from each other, throughout the entire area to be radiated. When gamma radiation alone is used, it should be borne in mind that the greater the distance the radium is placed from the surface, the greater the relative penetration secured in the depths. The ideal radiation is a homogeneous and equal one throughout the entire affected volume.

Consideration of the above facts makes it clear why to do extensive work adequate amounts of radium are necessary, and why the statements of so many milligram hours with such and such filters mean little or nothing unless the distance worked at is clearly stated. It is also, we think, evident that each must be individualized and appropriate radiation given. In cancers along the vaginal wall, especially on the rectal side, it is of advantage to have flat applicators and to get within a few millimeters of the vaginal surface, as in this way the infected vagina gets a maximum and the rectum a minimum radiation. In radiating the regional lymphatic glands or upper parametrium, a number of portals should be used from the abdomen, back, vagina and perineum, at distances varying from 2 to 5 inches from the surface. Figures 3 and 4 show schematically the common locations and distances of the cervical and vaginal cancers from the body surface. We propose in a separate communication to deal exhaustively with the technic of radiation and will not go into further detail here.

Excellent descriptions of the histopathologic changes found in the cancerous uterine cervix after intense radium radiation can be found in the reports of Hansemann[3] and Haendly.[4]

Beginning a week after radiation there is swelling of the cell protoplasm, hyperchromatosis and pyknosis of the nuclei. After five or six weeks, the cancer cells are entirely gone, the connective tissue and blood vessels show hyaline changes. There may be a marked infiltration with polymorphonuclear leukocytes, and often giant cells are

3. Hansemann: Berl. klin. Wchnschr., 1914, No. 23, p. 1061.
4. Haendly: Berl. klin. Wchnschr., 1914, No. 2, p. 86.

present. At a later stage this necrotic and inflammatory tissue is replaced by ordinary connective tissue. When radium is placed directly within the cervix and left sufficiently long, changes of this type invariably occur.

We have eight uteri removed a sufficient time after radiation to study the changes in the tissues. Vestiges of cancer have been demonstrated in only three of these. All will be serially sectioned and reported on in detail in a later communication. All were from patients with cancers originally inoperable.

It should be borne in mind that the intense inflammatory changes described above follow overradiation and are due to imperfect technic. The action of the rays is not in a true sense specific; normal tissues as well as pathologic are injured and can be easily destroyed. There are wide variations in the resistance to radiation in different normal tissues. The vaginal wall and cervix are very resistant, enormously more so than skin. Bumm of Berlin gave currency to a widely accepted dictum that the limit of the gamma-ray efficiency (in tissue) was 4 cm. It is probably true that it is not possible to place radium ridectly in the cervix and radiate sufficiently to destroy the cancer cells beyond 4 cm. without causing severe local destruction of normal tissues; but it is possible to radiate from almost any distance by proper disposal of the applicators. In one case we cleared up an extensive vaginal cancer by radiation through the vulva, the radium being placed 10 cm. from the surface of the vulva. In another patient who did not recover, but died of general cancer, we saw large metastatic deposits disappear from the iliac lymphatic glands—the patient was thin and the masses easily outlined.

Our view of the action of radium is that, to markedly varying degrees, it injures all tissues, and that the injury is some kind of intracellular chemical change. It seems to us improbable, however, that the disappearance of cancer cells without any demonstrable effect on normal cells can be due solely to a difference in resistance of the cells to radiation. The common observation that in two cases with the same type of growth, subjected to the same radiation, different results are obtained; that in one the cancer disappears promptly and in the other is not affected at all, suggests the importance of resistance in the patient. It also opens up a wide field for speculation and experimental investigation as to what this resistance may be, where it is located, how it may be artificially produced, etc.*

Radiation carried to the extent of severe injury of normal tissue may defeat its own ends. We have observed in one specimen of uterine cancer and several specimens from other parts of the body a condition which needs interpretation. In the cervix cancer the facts are as follows: The patient came in with solidly fixed parametria; intense intracervical radiation was given with the result that the uterus became freely movable; after six weeks hysterectomy was performed. Microscopic study showed from within outward, (1) a zone of necrosis; (2) a zone of greatly modified connective tissue, blood vessels and altered cancer cells; (3) a zone of normal connective tissue and no cancer cells.

In every patient treated, a radiation up to but not beyond this toleration of the normal tissues should be given so as to take in all the infected area, including the parametria and regional lymphatic

*See abstract of article by J. B. Murphy and J. J. Norton under Reviews and Abstracts in this number.—Ed.

territory. This radiation should be made as homogeneous as possible, bearing in mind the underlying physical principles already mentioned.

The most easily injured normal tissue in connection with cervical and vaginal cancer radiation is the rectum. In our earlier cases, when we were less familiar with our agent and totally unacquainted with the tissue reactions, this complication was not uncommon and in some cases led to such serious results as ulceration, fistula formation and even death from infection. Such a complication manifests itself first in from ten days to two weeks after the application, by diarrhea and tenesmus. In the mild types this may disappear in two weeks and no further trouble develop. In the severer grades the proctitis lasts two months or more, then disappears to recur about the beginning of the sixth or seventh month, with ulceration in the anterior rectal wall. This condition is very painful and takes from three to five months to heal. In the worst cases actual fistula formation takes place before healing. *We are happy to state that this complication can be avoided in every case.* We have not seen it for months.

The first radiation should be given in a single dose, following which a pause of at least five or six weeks is necessary before a second treatment is given. During this time the patient should be examined once a week. Some carcinomas, especially the basal celled of the vaginal wall, begin diminishing in a few days and disappear in as short a period as two weeks after the treatment. Most of them begin the decrease at the end of two weeks and continue diminishing for five or six weeks. If at the end of six weeks the growth has disappeared, another four weeks should pass before a second treatment is given. After the second treatment practically all cases in which there will be recovery will show complete disappearance of the growth. In view of the fact that we have seen a number of recurrences developing several months after apparent complete disappearance of the growth, we believe that the radiation should be repeated every few months for a year or two. Some of our permanent successes have been, however, secured from a single radiation.

As a rule, the general symptoms which follow a radiation are mild nausea for twenty-four hours and a sense of weakness for four or five days. Sometimes there are no disagreeable symptoms at all, and in no case has there been any alarming developments. The patients are rarely kept in the hospital longer than the day of treatment.

Every patient before treatment is most thoroughly investigated both from the local and general standpoints, and invariably tissue is secured for microscopic study. The application of the radium sometimes made under nitrous oxid is more frequently made without anesthesia.

Up to the present time we have not found means of determining prior to radiation what its effect will be. The general strength of the patient is not of prime importance. We have seen local disappearances in patients in the last stages of general carcinomatosis. Nor is the extent of local involvement of importance; large growths may disappear and small ones fail to do so. The histologic type is likewise relatively unimportant in this connection; in the cured list are twenty-nine squamous-celled epitheliomas, seventeen basal-celled epitheliomas and seven adenocarcinomas. In passing, we desire to state that squamous-celled epitheliomas may long remain local, and that some basal-celled epitheliomas rapidly metastasize. Among the recurrent cases, it has been noted that those which develop late, two years or more after operation, almost always do well; the cause most likely is connected with immunity factors in the patient.

CLASSIFICATION AND DEFINITION.

We have divided our cases into three groups: 1, operable; 2, inoperable; 3, recurrent inoperable. The results obtained have also been placed in three classes: 1*a*, clinically cured; 2*a*, improved; 3*a*, unimproved.

1. By operable cancers are meant those still confined to the cervix or only moderately involving the parametria and vaginal walls. They are not fixed to the pelvic wall on either side and have not caused hydronephrosis and are not associated with pelvic pain.

2. By inoperable cancers are meant those associated with general metastasis, those firmly fixed to one or both pelvic walls; those extensively involving the bladder, vagina or rectum. In short, cases in which we have never cured the patients by operation.

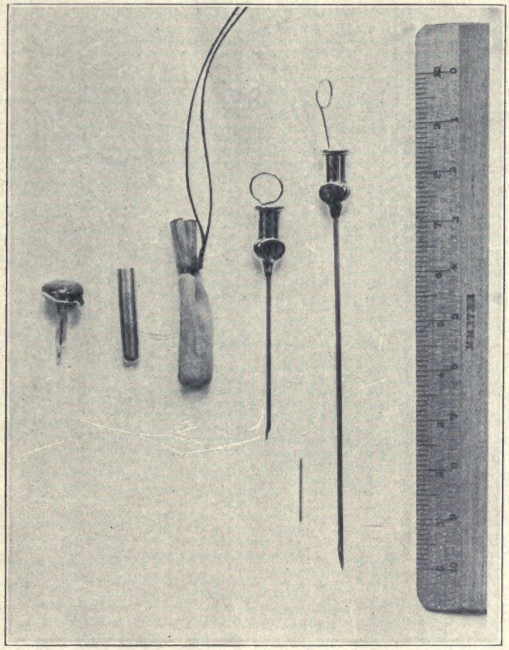


Fig. 1.—Radium applicators and scale indicating size.

3. By recurrent inoperable cancers are meant such recurrences following operation as we have never cured except by radium.

1*a*. By clinically cured is meant the complete disappearance of the cancer so far as palpation, curettage or other method may disclose associated with the apparent perfect general health of the patient.

2*a*. By improved is meant a definite betterment of the patient's condition. In the lesser degrees this may consist of a cessation of hemorrhage and discharge, or a disappearance of pain which has resisted all the drugs, including morphin. Among these, too, are placed twelve cases in which all local trouble disappeared, but the patient showed

metastasis at the time of treatment or developed it subsequently. Two of these patients were found locally free of cancer at necropsy, and in two, in whom hysterectomy was carried out after apparent clinical cure, the uteri are clear of the disease, in spite of the fact that both patients are now dead from general metastasis. In most of the cases of this group the reduction in the size of the tumor was marked. It also includes some early cases in which the treatment was very imperfect.

3*a*. By unimproved is meant no material benefit having been produced. Most of these showed histologic improvement on microscopic examination of curettings. In more than two thirds of them the disease was immense and the general condition of patients bad.

All of the patients included in this report were treated prior to January, 1915, and the cured ones were apparently cured at that time. All of the cured have been investigated by one or both of us personally, with a few exceptions in which the examinations were made by competent men. The last report on each case was obtained in May, 1915.

Results.

The results obtained by the treatments may be summarized as follows:

Out of the 213 cases treated, 14 were operable and 199 inoperable.

Operable Cases.—Of the 14 operable cases, 10 patients were operated on and treated prophylactically with radium. Of these, 2 have been well for more than three years, 1 for more than two years, 4 for more than a year, and 3 for more than six months. The number is too small to draw conclusions from, and yet is suggestive, when we consider that in 75 per cent. of all cases with operation there is recurrence and that 60 per cent. of these recurrences take place within one year following the operation.

In four cases of the operable group, on account of some general contraindication to operation, radium alone was used. All of this group are living and well; 2 for over three years and 2 for over one year.

Inoperable Cases.—The total number of inoperable and inoperable

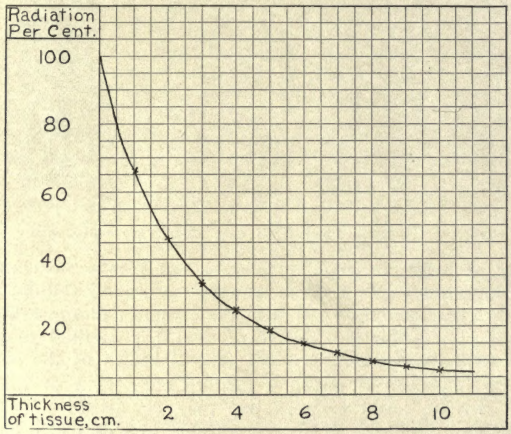


Fig. 2.—Curve showing the variation of the intensity of gamma radiation with the thickness of tissue.

recurrent cases is 199, of which 53 patients have been clinically cured, 109 markedly improved and 37 not improved.

Our series includes 35 cases of originally inoperable cancer of the cervix uteri or vagina in which the patients are clinically cured; in 2 cases for over four years; in 2 case for over three years; in 4 cases for over two years; in 17 cases for over one year; in 10 cases for over six months. It also includes 18 cases of originally inoperable recurrent cancers in which the patients are now clinically cured; in 1 case for over six years; in 1 case for over four years; in 11 cases for over two years; in 10 cases for over one year; in 5 cases for over six months.

Fig. 3.—Common locations and distances of the cervical and vaginal cancers from the body surface as seen from the side.

Excluding the operable cases, in which we have both operated and used radium, there are 203 cases left; in 57 of these 203 cases the patients are clinically cured. We employ the word clinically cured and will reserve the word cured for later reports, to apply to cases beyond the five-year limit, which has been conventionally adopted by surgeons as a time limit for estimating the permanency of cures of malignant disease.

Of the 57 clinical cures, 1 has lasted for six years; 3 for over four years; 4 for over three years; 5 for over two years; 29 for over one year, and 15 for over six months.

Conclusions.

We are convinced that radium is of exceedingly great value in the treatment of cancers of the cervix uteri and vagina.

We expect with all confidence that the results in the next 200 cases will far surpass those reported here.

We again emphasize that the betterment in the improved but not

cured cases is so marked that it alone makes radium a great addition to existing methods and would justify its use.

We believe that every inoperable cancer of the cervix uteri or vagina, provided general metastasis is not evident, stands a chance of at least 1 in 4 of cure by radium treatment.

There is a marked reason to believe not only that a large number of inoperable cases are curable, but that by the joint use of radium and operation that the 1 in 4 cure rate of operation in operable cases may be raised to 3 in 4 or better.

We have seen that some cervical cancers do not respond to radium treatment. This same variation in reaction occurs in many other types of neoplasm. It is apparently due to a lack in the patient of resistance to the specific growth. Work should be directed toward determining where the body products which attack a radiated cancer arise and what they are. On account of the certainty that some of the operable cancers of the cervix would not be cured by radium and also on account of the necessity of having many patients over five years cured in order to be sure of the permanency of the results, we advise, in operable cases, hysterectomy and radiation. This is the rule in clearly operable conditions. In border-line cases, we advise the use of radium, as the permanent cures from operation are not numerous in this group. If the growth does disappear, it can only be determined whether or not hysterectomy is advisable by trying out both methods; this as yet has not been done in a sufficient number of cases to arrive at any definite conclusions. We do feel, however, that when clinical cures have occurred in inoperable cases, operations are probably best not carried out. Manifestly an inoperable case which becomes operable but does not entirely heal should be treated by operation.

Finally we desire to restate most emphatically that radium can and should be used in these cases without any local or general injury to the patient treated.

1418 Eutaw Place.

Fig. 4.—Common locations and distances of the cervical and vaginal cancers from the body surface as seen from the front.

REVIEWS AND ABSTRACTS.

James B. Murphy and John J. Norton. The Effect of X-ray on the Resistance to Cancer in Mice. Science N. S. Vol. XLII, No. 1093, pp. 842-3. (From the Laboratories of The Rockefeller Institute for Medical Research. Abstract of paper presented at the New York meeting of the National Academy of Sciences.) "It has been shown in previous communications that the resistance to heteroplastic tissue grafts apparently depends on the activity of the lymphocyte. The facts on which this conclusion is based are briefly as follows: The chick embryo, which normally lacks the ability to destroy a heteroplastic tissue graft, if supplied with a bit of adult lymphoid tissue, becomes as resistant as the adult in this respect. Furthermore, an adult animal deprived of the major portion of its lymphoid system by repeated small doses of X-ray, no longer has the power to destroy a graft of foreign tissue, and this tissue will grow actively. The chief characteristic of a failing heteroplastic graft in the unsuitable host is a marked local accumulation of lymphocytes. The histological picture is identical in a failing cancer graft in an immune animal of the same species. Synchronous with the establishment of the cancer immunity and during the period in which the lymphocytes are accumulating around the cancer graft, there is a lymphocytic crisis in the circulating blood. This is found in the actively immunized animals as well as in those possessing a natural immunity, but is totally lacking in animals susceptible to the cancer graft. If the lymphoid crisis be prevented in immune animals by a previous destruction of the lymphoid elements with X-ray the potentially immune animal is changed to a susceptible one."

"We have noted that while repeated exposures to X-ray will destroy the lymphoid elements of an animal, one small dose will stimulate these same cells. With this artificial method of producing a lymphocytosis we have attempted to study the relation of this condition to the resistance of mice to their own spontaneous tumors. For evident reasons it was necessary to rule out the complicated question of the direct effect of X-ray on the cancer. In order to do this we have removed the cancer at operation, and with the cancer out the animal has been subjected to a stimulating dose of X-ray. Immediately after this a graft of the original tumor was replaced in the groin of the animal. As a control the same procedure was carried out, but with X-ray treatment omitted. As a further check to the results cancers were removed from a number of animals and in this set the cancers were exposed directly to the same amount of X-ray that the animals in the first group received. After this a graft of the tumor was returned to the original host."

"The results of these three experiments are to be judged by two criteria. First, whether or not there is a return of the disease, either at the site of removal of the cancer, or at the point of inoculation of the returned graft; and second, the time at which the returned graft starts in active growth, if at all, the figures on these points are given in the following table."

	Immune Per Cent.	Susceptible Per Cent.	Local Recurrence of Tumor Per Cent.	Average Time for Appearance of Graft.
Series I.	50.0	50.0	21.2	5 wks. and 4 days.
Series II.	3.4	96.6	48.3	1 wk. and 5 days.
Series III.	0.0	100.0	40.0	1 wk. and 3 days.

"Series I. was composed of 52 animals treated by X-ray while the

cancer was outside of the body, with later a return of a graft of the tumor. Series II. was made up of 29 control animals in which the cancer was removed and a graft returned without treatment to either animal or tumor. Series III. was made up of ten animals from which the cancer was removed and the cancer subjected directly to the same amount of X-ray that the animals received in the first series, and later a graft of this X-rayed cancer returned to its original host."

"It will be seen from these figures that an X-ray dose which produced a lymphocytosis when administered direct to the animal was sufficient to render 50 per cent. of the mice so treated immune to a returned graft of their own tumor, and in the other 50 per cent. greatly to retard the return of the disease. A similar dose of X-ray given to the cancer direct outside of the body did not influence the subsequent growth of a graft of this tumor when returned to its original host. The contrast between these figures and those of the control series is striking, as is also the number of local recurrences in the two series. If this pronounced result is obtained with one stimulating dose it is probable that a more pronounced effect might be obtained by a second exposure to X-ray after a suitable interval."

* * * * *

D. T. Quigley, M.D. (Omaha). Preliminary Report of a Large Angiomatous Tumor in Baby, Treated by Radium. Western Medical Review, April, 1915, pp. 235-6. "On January 8, 1915, the baby was sent to Omaha for radium treatment. The baby was two weeks old and had an enormous tumor, half the size of its head, in the axilla. The tumor had doubled in size during the two weeks of the child's extra uterine life and was therefore growing so rapidly that the baby's life was in danger from this rapid growth. The baby had lost weight since birth so was in a dangerous condition."

"The histo-pathology of the tumor is not known, as owing to extreme vascularity it was impossible to remove a piece for the microscope, but this vascularity was great enough to make it almost certain that the main structure of the thing was angioma. There were islands of harder tissue to be felt through the mass which I consider fibrous or fibroid tissue. When the baby cried the mass became turgid and bluish, showing the large blood supply. Owing to the tender age of the baby and the danger of hemorrhage, operation was considered out of the question. The danger of hemorrhage also made it impossible to bury radium in the mass. It was therefore decided to treat the tumor by cross-fire from the outside. In giving the treatment great care was exercised to avoid a dose in any place that might cause enough destruction of tissue to break into one of the blood vessels and thereby cause hemorrhage. The radium was used with a combination of distance and metal filtration and by the cross-fire method, nearly every night for three weeks. The dose was gauged somewhat according to the constitutional reaction and the amount used was from 5 to 50 milligrams of radium. This is a large dose for a baby, but considering the large size of the tumor and the fact that young people stand the constitutional reaction well, I felt justified in using it."

"The tumor began to shrink in size so rapidly that at the end of the first week it had gone down one inch in size. At the end of the third week it was about half the size it had been when treatment was begun. At this time, considering that it had had the maximum dose, the family returned to South Dakota. A letter from Dr. Embree of recent date states that the tumor is still undergoing retrogression and

the baby is gaining in weight and doing well in every way. I expect the whole mass to disappear under the radium treatment, but if this does not occur and a small hard fibrous mass is left, the danger point has been passed. The baby has grown in strength, the blood vessels that held the threat of hemorrhage have been destroyed, and if operation becomes necessary to remove the remains of the mass it can now be done safely."

"A letter dated June 2, 1915, states: "The tumor is now the size of an egg cut in two."

CONTRIBUTION ON THE THERAPEUTIC VALUE OF THE INTRAVENOUS INJECTION OF SOLUBLE RADIUM SALTS IN THE TREATMENT OF PERNICIOUS ANAEMIA AND LEUKAEMIA.

BY FREDERICK PROESCHER, M.D. AND B. R. ALMQUEST, M.D.

The marked stimulating effect of the radioactive substances in relatively small doses upon the erythrocytes and the destructive effect of large doses upon the leucocytes makes them valuable therapeutic adjuvants for the symptomatic treatment of the various forms of anaemia, especially pernicious anaemia and leukaemia.

The general opinion that all radioactive substances have a similar biological action is true only with certain restrictions. While all produce a more or less marked numerical increase of the red cells, the destructive effect upon the leucocytes is only pronounced in the case of thorium-X.

Radium shows a less destructive action on the leucocytes than thorium-X, when compared on the basis of their activity units.

Our animal experiments have demonstrated that radium in superfatal doses is unable to destroy all the circulating leucocytes or lymphoid-myeloid cells of the bone marrow.

The difference in the biological effect between thorium-X and radium upon the leucocytes is probably only a qualitative rather than a quantitative one. The more rapid decay of thorium-X as compared to that of radium explains its more intense biological action. The alpha rays have no doubt the most intense biological action on both the white and red cells, because they are easily absorbed and retained, while the hard beta and gamma rays are less effective, probably due to their great penetrating properties, that is, they are not intercepted by the cell structure.

The action of radioactive substances on the blood cells, especially on the red cells, is at the present time an unsolved problem. There can be no doubt that the red cells are far more resistant than the leucocytes as a complete destruction of the red cells under experimental conditions, in spite of using superfatal doses, was not observed.

We treated one case of essential pernicious anaemia (Morbus Biermer) (Case I.) and one case of generalized infectious lymphadenitis, with enlarged spleen of unknown origin, with a pernicious anaemic blood picture (Case II.) and a case of myeloid leukaemia (Case III.)

Before entering into the discussion of our cases, we will give the case histories and the results of the blood examinations.

Case I.—Mr. W., age 52 years, occupation, oil driller. Patient first noted symptoms of the disease October, 1912. He became pale and

weak and was reported to us by Dr. Mathewson, of Oakdale, Pa. The first blood examination was made December 1st, 1912, which showed 2,250,000 red cells, 65.1% haemoglobin and 6,250 white cells, color index 1.2. The differential count revealed a marked relative lymphocytosis. The microscopic aspect of the stained blood film showed macro and microcytosis, poikilcytosis and hyperchromasia of the red cells. No erythroblasts or gigantoblasts were noted. The physical examination as well as the clinical observation showed no signs of any organic lesions or helminthiasis which could account for the anaemia. We therefore dealt with a typical case of Morbus Biermer.

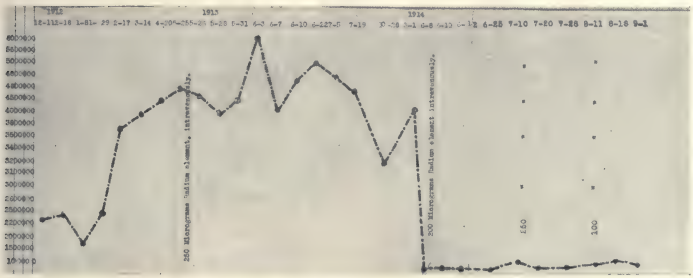
The patient received 2 grains of cacodylate of soda daily from December 7, 1912 to May 7, 1913, and from January 21, 1913 to May 7, 1913 was given an arsacetin solution prepared as follows:

7½ grains arsacetin were dissolved in 1 c.c. distilled water and the solution sterilized for 10-15 minutes in a steam sterilizer. One half of the solution was given on the day of preparation, the remainder the following day. The injections were repeated every third or fourth day. On may 25, 1913, he received the first radium injection, of 250 micrograms of radium element intravenously. From November 22 to December 22, 1913, the patient again received a series of ten injections of arsacetin. On July 10, 1914 and August 11, 1914, patient received 250 and 100 micrograms of radium element intravenously and from June 10, 1914 to August 11, 1914, again 8 grams of arsacetin. Altogether he received a little over 18 grams of arsacetin and 600 micrograms of radium element. The patient died June 14, 1915. An autopsy was not permitted. The following tables and charts show the influence upon the blood picture:

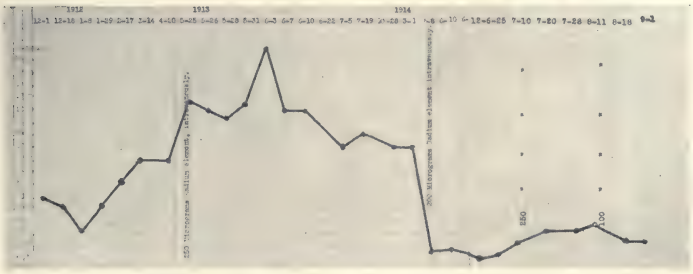
CASE I.

Date.	Haemoglobin. Grams.	Haemoglobin. %	Red Cells.	Color Index.	White Cells.	Neutrophiles.	Eosinophiles.	Basophiles.	Lymphocytes.	Monocytes.
12- 1-12	9.12gm.	65.1	2250000	1.2	6250	46.00	3.00		51.70	
12-18-12	8.52gm.	60.8	2350000	1.2	8500	57.00			43.00	
1- 8-13	6.56gm.	46.8	1575000	1.4	6560					
1-29-13	8.24gm.	58.9	2300000	1.2	8400					
2-17-13	10.24gm.	73.1	3750000	0.9	6000	49.55	4.42		46.20	
3-14-13	12.24gm.	87.4	4000000	1.1	5400	43.00	2.00		58.00	
4-20-13	11.96gm.	85.4	4500000	.9	1000	45.00	1.00		54.00	
			Before injection of Radium.							
5-25-13	16.76gm.	119.7	4600000	1.3	5620	44.46	2.36	1.59	42.79	
			12:53 P. M. ¼ mgr. Radium Bromide given intravenously.							
			2:10 P. M. after injection of Radium.							
5-25-13	16.44gm.	117.4	4443000	1.2	5500	56.02	1.33	0.66	40.33	1.66
5-26-13	16.70gm.	119.3	4550000	1.3	7000	56.49	2.75		41.12	9.64
5-28-13	15.56gm.	111.1	4050000	1.3	7750	47.90	0.96	0.96	45.64	4.50
5-31-13	16.46gm.	117.5	4550000	1.3	9250	53.22	3.03	0.60	36.47	6.68
6- 3-13	21.44gm.	153.1	6050000	1.2	6500	48.00	3.73	0.53	41.86	5.86
6- 7-13	16.16gm.	115.4	4132000	1.4	5000	41.58	1.90		51.74	4.76
6-10-13	16.44gm.	117.4	4700000	1.2	17500	46.90	2.27	0.56	46.87	3.40
6-22-13			5000000		5500	47.85	2.90	0.87	42.26	6.12
7- 5-13	13.16gm.	94.	4800000	.9	8125	49.38	1.66		46.63	2.33
7-19-13	14.04gm.	100.3	4500000	1.1	7000	46.01	2.66		48.33	3.00

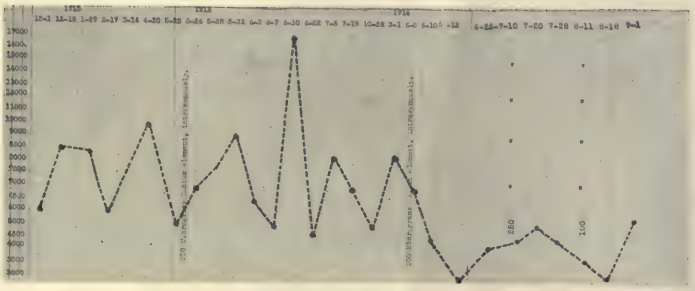
10-28-13	13.76gm.	98.2	3200000	1.5	5000	51.56	1.90		45.35	1.19
3- 1-14	13.16gm.	94.	4250000	1.1	8250	55.80	2.30	0.30	35.30	6.30
6- 8-14	4.78gm.	34.1	1376000	1.3	7000	71.50	2.00		20.50	6.00
6-10-14	4.78gm.	34.1	1336000	1.3	4500	51.50	1.50		39.00	8.00
6-12-14	4.48gm.	32.	1352000	1.1	3000	49.00			48.00	3.00
6-25-14	3.42gm.	24.4	1152000	1.+	4280	43.00			57.00	
7-10-14	5.08gm.	36.3	1520000	1.2	4500	60.00	1.00	1.00	36.00	2.00
		250 Micrograms Radium element intravenously.								
7-20-14	6.25gm.	44.6	1300000	1.7	5000	53.50	1.00	1.50	42.50	1.50
7-28-14	6.00gm.	42.9	1476000	1.4	5000	68.50	1.00	1.50	29.00	
8-11-14	6.58gm.	47.	1448000	1.6	3750	57.00	1.00		42.00	
		100 Micrograms Radium element intravenously.								
8-18-14	5.38gm.	38.4	1656000	1.1	2750	55.00	3.00	1.00	40.00	1.00
9-15-14	5.82gm.	41.5	1484000	1.9	3750					
10-23-14	3.14gm.	22.4	1500000	.6	5250	52.00	1.00	1.00	46.00	
3- 9-15		40.	1084000	1.8	4100	61.60	.60		35.20	1.40



Case No. 1.—Red Cells.



Case No. 1.—Haemoglobin.



Case No. 1.—White Cells.

Case No. 2. Mr. St. K., aged 21, Slavish, occupation laborer. Referred by Dr. A. Petit. No intelligent history could be obtained. Patient noticed that during the past several weeks he was getting weaker and pale. A blood examination on April 13, 1914, showed: red cells 1,376,000, white cells 8,500, haemoglobin 27.7%. Stained blood films and differential count showed a pernicious anaemic blood-picture. He was treated only with intravenous radium injections and received 500 micrograms of radium element. After the last radium injection the patient did not return, and therefore, further blood examinations could not be made.

Case No. 2.

Date.	Haemoglobin Grams	Haemoglobin %	Red Blood Cells.	Color Index.	White Blood Cells.
4-13-14	3.88	27.7	1,376,000	1.2	8500
4-14-14	5.40	38.6	1,414,750	1.3	10750
	400 Micrograms Radium element intravenously.				
4-15-14	4.78	34.1	1,562,500	1.1	11000
4-16-14	5.38	38.4	1,848,000	1.0	7312
4-18-14	6.88	49.1	1,776,000	1.3	4000
4-20-14	5.52	39.4	1,824,000	1.1	5000
4-22-14	6.42	45.9	2,200,000	1.4	4315
4-25-14	7.18	51.3	2,520,000	1.1	4000
4-28-14	10.76	76.9	2,608,000	1.4	4875
5- 1-14	11.06	79.0	2,992,000	1.3	5000
5- 5-14	10.16	72.6	2,776,000	1.4	6750
5- 7-14	10.16	72.6	2,872,000	1.2	6750
5-13-14	9.84	70.3	2,800,000	1.2	10480
	100 Micrograms Radium element intravenously.				
5-15-14	9.56	68.3	3,152,000	1.0	10320

Case No. 2.

MICROSCOPICAL ASPECT OF STAINED BLOOD FILMS

4-13-14—Macro and microcytosis, poikilocytosis, few polychromatic red cells. Hypo and hyperchromasia of red cells. Few platelets.

4-14-14—Macro and microcytosis, poikilocytosis, hypo and hyperchromasia of red cells.

4-15-14—Macro and microcytosis, hypo and hyperchromasia of red cells. Few platelets.

4-18-14—Macro and microcytosis, slight poikilocytosis, slight polychromasia of red cells.

4-18-14—Slight macro and microcytosis, poikilocytosis, many polychromatic red cells. Few platelets.

4-20-14—Slight poikilocytosis, macro and microcytosis, few polychromatic red cells. Very few platelets.

4-22-14—Macro and microcytosis, slight poikilocytosis, many polychromatic red cells. Very few platelets.

4-25-14—Macro and microcytosis. Very few platelets.

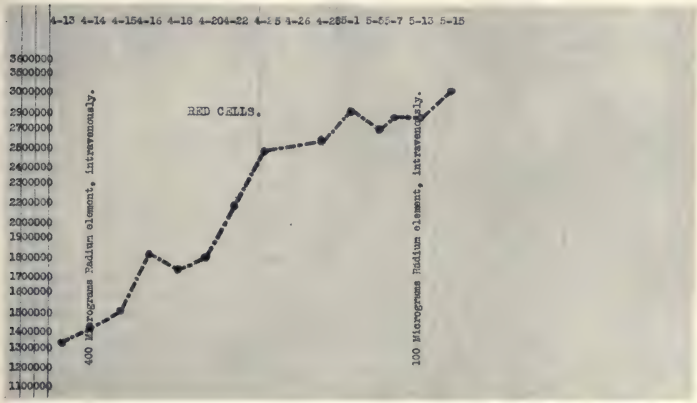
5- 1-14—Macro and microcytosis, slight polychromasie of red cells. Slight poikilocytosis, microcytes show marked hyperchromasia.

5- 5-14—Slight macro and microcytosis, many polychromatic red cells. Hyperchromasia of microcytes. Few platelets.

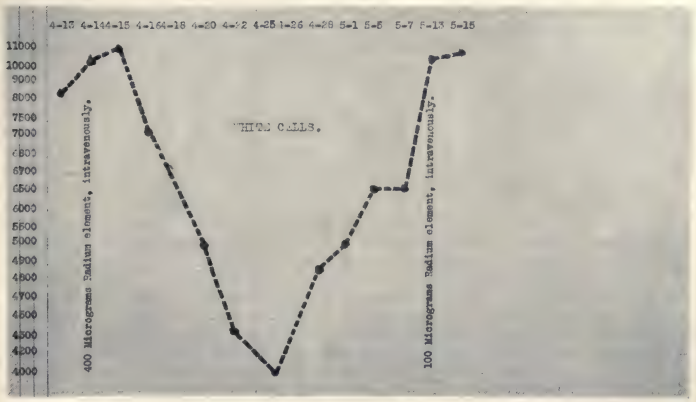
5- 7-14—Slight poikilocytosis. Many polychromatic red cells. Few platelets.

5-13-14—Slight macro and microcytosis. Slight poikilocytosis. Few hyperchromatic red cells. Few polychromatic red cells. Few platelets.

5-15-15—Slight macro and microcytosis. Few hyperchromatic red cells. Few polychromatic red cells. Few platletes.


4-13 4-14 4-15 4-16 4-18 4-20 4-22 4-25 4-26 4-28 5-1 5-5 5-7 5-13 5-15
RED CELLS.
400 Micrograms Radium element, intravenously.
100 Micrograms Radium element, intravenously.

Case No. 2.—Red Cells.


4-13 4-14 4-15 4-16 4-18 4-20 4-22 4-25 4-26 4-28 5-1 5-5 5-7 5-13 5-15
WHITE CELLS.
400 Micrograms Radium element, intravenously.
100 Micrograms Radium element, intravenously.

Case No. 2—White Cells.

Case No. 2.

DIFFERENTIAL COUNT—CASE NO. 2.

Date.	4-13-14	4-14-14	4-15-14	4-16-14	4-18-14	4-20-14	4-22-14	4-25-14	4-28-14	5-1-14	5-5-14	5-7-14	5-13-14	5-15-14
Poly-Neutrophiles.	19.45	13.89	16.50	18.00	24.89	22.26	14.50	21.36	32.50	36.25	34.73	25.69	23.06	21.75
Poly-Eosinophiles.	0.50	2.25	2.00	.00	1.90	0.82	1.00	.00	1.00	1.35	0.53	0.47	0.27	1.39
Basophiles.	.00	.64	.00	.00	.42	.00	.00	.50	.00	.00	.00	.00	.27	.00
Lymphocytes (small)	67.50	35.58	27.50	36.50	38.26	39.07	49.00	29.54	26.40	29.41	24.68	47.14	36.43	33.78
Lymphocytes (m'd'm)	14.50	11.22	11.50	11.00	9.54	8.82	7.50	5.49	13.50	22.21	13.36	9.90	16.43	25.04
Micro-Lymphocytes.	2.50	4.83	9.50	3.50	6.87	3.36	6.50	29.09	3.50	.00	1.60	2.90	4.10	7.40
Meta-Myelocytes.	.00	1.62	1.50	.00	.00	2.94	.00	1.36	2.50	.00	9.03	4.76	.00	.46
Neutro.-Myelocytes.	1.00	.03	.00	.00	.00	.00	.00	.00	.50	.00	.00	.00	.00	.00
Myeloblasts.	.00	2.25	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00	.00
Leucoblasts.	.00	.00	5.00	3.50	3.23	.82	4.00	1.31	2.50	.00	1.01	.00	.54	.00
Monocytes.	.00	7.09	7.00	6.00	.00	2.25	.00	.00	1.00	.00	.00	.00	.82	1.85
Erythro-blasts. Gigantoblasts.	.00	20.32	19.50	21.50	15.27	17.97	17.50	11.40	7.00	9.95	14.43	9.04	18.08	8.33

4-13 4-14 4-15 4-16 4-18 4-20 4-22 4- 5 4-26 4-28 5-1 5-5 5-7 5-13 5-15
400 Micrograms Radium element, intravenously.
HAEMOGLOBIN.
100 Micrograms Radium element, intravenously.

Case No. 2.—Haemoglobin.

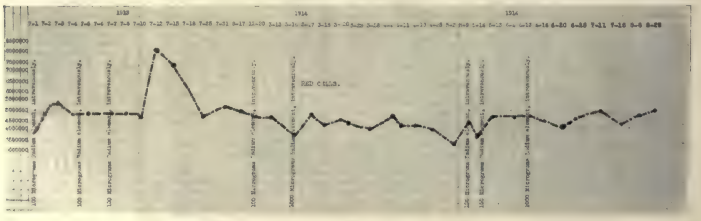
Leukaemia Case.

Case III. Mr. A., age 33 years, occupation, railroad clerk. In August, 1911 the patient noted an enlargement of the abdomen. Six months later a greatly enlarged spleen was found and a blood examination showed a leukaemic ccondition. The spleen was extirpated March, 1912, by Dr. Campbell, and the patient made a complete recovery as far as the operation was concerned. We saw the patient July 1, 1913, and a blood examination on the same day showed; 222,500 white cells, 4,087,500 red cells and 91.7% haemoglobin. The differential count showed a myeloid leukaemia. He was treated with intravenous radium injections and received the following amounts of radium element: From July 1, 1913 to July 7, 1913, 400 micrograms in fractional doses of 100 micrograms every second day, on December 20, 1913, 100 micrograms; on March 16, 1914, 1,000 micrograms (1 milligram); on May 9, 1914, 100 micrograms; on May 16, 1914, 100 micrograms, and on June 13, 1914, 1,000 micrograms (1 milligram). On 8-31-14 the patient was radiated for 3½ hours with 300 mgm. of radium element, and between 9-26-14 and 11-4-14 he received eleven X-ray treatments. The patient died January 15, 1915. An autopsy was not permitted.

Case No. 3.

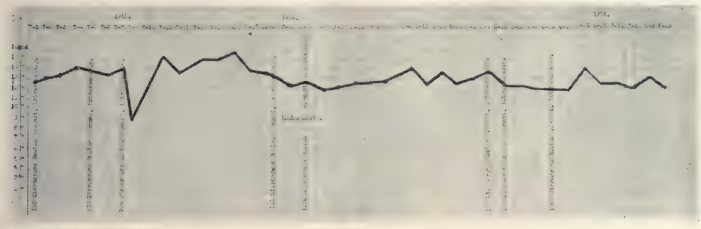
Date	Haemoglobin.	Percentage.	Red B. Cells.	Color Index.	W. B. Cells.
7- 1-13	12.84gm.	91.7	4,087,500	1.1	222,500
	100 Micrograms Radium element intravenously.				
7- 2-13	13.16gm.	94.	5,725,000	0.8	272,500
7- 3-13	13.16gm.	94.	5,656,000	0.8	223,125
	100 Micrograms Radium element intravenously.				
7- 4-13	14.04gm.	100.3	4,900,000	1.0	267,500
7- 5-13	14.36gm.	102.6	4,900,000	1.0	280,000
	100 Micrograms Radium element intravenously.				
7- 6-13	13.76gm.	98.3	5,050,000	0.9	266,000
7- 7-13	13.96gm.	99.7	4,900,000	1.0	245,000
	100 Micrograms Radium element intravenously.				
7- 8-13	8.96gm.	64.	4,885,000	0.6	265,000

Date	Haemoglobin.	Percentage.	Red B. Cells.	Color Index.	W. B. Cells.
7-10-13	7.44gm.	53.1	4,600,000	1.0	242,500
7-12-13	15.24gm.	108.9	8,350,000	0.6	231,200
7-15-13	13.76gm.	98.3	7,500,000	0.6	225,000
7-18-13	14.96gm.	106.9	6,450,000	0.8	270,000
7-25-13	14.96gm.	106.9	4,850,000	0.8	305,000
7-31-13	15.56gm.	111.1	5,400,000	1.0	292,500
8-17-13	13.76gm.	98.3	5,300,000	0.9	255,000
12-20-13	13.44gm.	96.	4,950,000	0.9	350,000
		100 Micrograms Radium element intravenously.			
3-13-14	12.56gm.	89.7	4,778,000	0.9	214,000
3-16-14	12.56gm.	89.7	3,925,000	1.1	365,000
		1:30 P. M.—1,000 Micrograms Radium element intravenously.			
3-16-14	12.56gm.	89.7	4,128,000	1.0	260,000
		3 P. M.			
3-17-14	11.96gm.	85.4	4,088,000	1.0	255,600
3-18-14	12.24gm.	87.4	4,580,000	0.9	268,000
3-20-14	12.64gm.	90.3	4,640,000	0.9	250,000
3-23-14	12.56gm.	89.7	4,384,000	1.0	204,000
3-28-14	12.56gm.	89.7	4,280,000	1.1	200,000
4- 4-14	14.30gm.	102.1	4,825,000	1.1	142,500
4-11-14	12.56gm.	89.7	4,552,000	.9	118,000
4-18-14	13.76gm.	98.3	4,456,000	1.1	97,500
4-25-14	12.56gm.	89.7	4,240,000	1.1	105,200
5- 2-14	12.56gm.	89.7	4,440,000	1.1	124,700
5- 9-14	13.44gm.	96.	4,632,000	1.0	182,400
		100 Micrograms Radium element intravenously.			
5-16-14	12.56gm.	89.7	4,304,000	1.0	220,000
		100 Micrograms Radium element intravenously.			
5-23-14	12.56gm.	89.7	4,704,000	.9	200,600
6- 6-14	12.00gm.	85.7	4,768,000	.9	120,000
6-13-14	12.24gm.	87.4	4,896,000	.9	122,400
		1000 Micrograms Radium element intravenously.			
6-16-14	11.96gm.	85.4	4,736,000	.9	117,600
6-20-14	14.36gm.	102.6	4,424,000	1.1	109,600
6-28-14	12.56gm.	89.7	4,728,000	.9	112,000
7-11-14	12.56gm.	89.7	5,200,000	.8	115,000
7-18-14	11.96gm.	85.4	4,500,000	.9	91,000
8- 8-14	12.84gm.	91.7	4,864,000	.9	196,000
8-29-14	11.96gm.	85.4	5,152,000	.8	240,000
8-31-14					
		600 Milligrams Radium element, cross fire radiation to both femurs for 3½ hours each.			
9-12-14					182,000
9-19-14					158,000
9-26-14	14.04gm.		5,344,000		210,000
		Has had eleven X-ray Treatments.			
11- 4-14	11.64gm.	83.	4,664,000		167,000
11-30-14					117,600



Case No. 3.—Red Cells.

Case No. 3.—White Cells.



Case No. 3.—Haemoglobin.

Case No. 3.

DIFFERENTIAL COUNT.

	7- 1-13	7- 2-13	7- 3-13	7- 4-13
Poly-Neutrophiles	18.41	28.80	35.58	26.97
Poly-Eosinophiles	.90	.60	.25	.72
Basophiles	4.32	2.80	1.50	5.52
Meta-Myelocytes	15.16	11.60	11.50	13.96
Neutrophile-Myelocytes	33.39	36.20	29.50	29.16
Eosinophile-Myelocytes	.18	0.80	1.00	0.24
Myeloblasts	4.15	3.60	5.50	12.50
Leucoblasts	4.15	5.40	2.77	3.43
Large Lymphocytes	4.15	3.80	3.50	1.71
Medium	2.70	2.40	1.00	.24
Small	6.30	4.40	6.50	2.88
Micro	1.08	.20	1.00	1.71
Monocytes	1.26	.40		.72
	7- 5-13	7- 6-13	7- 7-13	7- 8-13
Poly-Neutrophiles	39.45	36.80	42.78	42.30
Poly-Eosinophiles		.12	.92	1.20
Basophiles		6.44	2.99	.72
MetaMyelocytes	12.94	8.13	9.30	7.80
Neutrophile-Myelocytes	30.25	22.00	24.18	28.78
Eosinophile-Myelocytes	0.48	0.22	0.23	2.88
Myeloblasts	7.10	6.44	5.34	4.08
Leucoblasts	2.20	.44	.23	1.92
Large Lymphocytes	.73			.96

Medium	2.20	2.80	2.53	2.40	
Small	3.92	15.55	9.89	6.24	
Micro	.48	.88	1.61	.48	
Monocytes	.24			.24	
	7-10-13	7-12-13	7-18-13	7-24-13	8-17-13
Poly-Neutrophiles	39.77	39.00	42.00	36.75	36.75
Poly-Eosinophiles	1.16	1.25	1.50	0.25	0.25
Basophiles	2.56		1.75	4.50	5.75
Meta-Myelocytes	11.88	5.00	12.00	7.00	4.50
Neutrophile-Myelocytes	23.31	37.50	19.50	30.00	29.00
Eosinophile-Myelocytes	1.16	5.00	.25	2.50	0.50
Myeloblasts	6.52	3.50	5.50	9.50	9.25
Leucoblasts	3.03	0.50	3.00	.75	3.25
Large Lymphocytes	2.09	0.25		1.50	1.00
Medium	1.16	2.50	2.25	3.75	2.50
Small	7.13	4.25	11.75	3.50	7.25
Micro		1.25	0.50		
Monocytes	.23				
	12-20-13	3-13-14	3-16-14	3-17-14	3-18-14
Poly-Neutrophiles	42.05	45.37	44.02	36.09	42.71
Meta-Myelocytes	15.00	7.33	10.00	20.33	19.33
Neutrophile-Myelocytes	3.33	1.66	7.33	00.00	1.66
Eosinophile-Myelocytes	00.00	00.00	00.00	00.00	00.00
Myeloblasts	19.33	00.00	1.33	3.33	1.33
Basophiles	4.66	2.33	3.00	3.66	2.33
Leucoblasts	2.66	4.00	5.66	7.00	17.66
Large Lymphocytes	0.66	7.66	5.00	2.66	0.66
Medium	4.66	25.33	14.33	14.33	6.33
Small	5.66	5.33	7.00	11.60	7.33
Micro	0.66	.33	1.00	1.00	0.66
Poly-Eosinophiles	1.33	0.66	1.33	00.00	0.00
Monocytes	0.00	0.00	0.00	00.00	0.00
	3-20-14	3-23-14	3-28-14	4- 4-14	
Poly-Neutrophiles	43.37	44.33	45.50	48.40	
Meta-Myelocytes	22.00	18.66	18.45	28.00	
Neutrophile-Myelocytes	00.00	00.33	00.00	00.00	
Eosinophile-Myelocytes	00.00	00.33	00.50	00.00	
Myeloblasts	00.66	00.33	03.00	05.10	
Basophiles	03.66	04.66	03.05	06.00	
Leucoblasts	11.66	15.27	13.50	2.50	
Large Lymphocytes	0.66	1.33	00.50	00.00	
Medium	16.00	9.33	2.00	3.50	
Small	1.33	1.66	8.50	2.50	
Micro	00.00	00.00	00.00	1.00	
Poly-Eosinophiles	0.66	1.00	2.00	2.50	
Monocytes	00.00	00.00	3.00	0.50	
	4-11-14	4-18-14	4-25-14	5- 2-14	
Poly-Neutrophiles	48.33	45.00	51.37	45.37	
Meta-Myelocytes	16.70	21.33	17.66	17.66	
Neutrophile-Myelocytes	00.00	00.00	00.00	00.00	
Eosinophile-Myelocytes	00.00	00.00	00.00	00.00	
Myeloblasts	7.00	4.33	2.33	3.66	

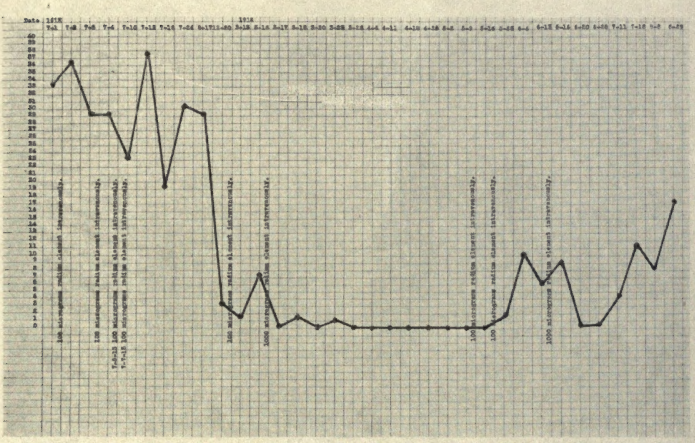
Basophiles	5.00	3.66	3.00	6.33	
Leucoblasts	10.66	8.04	3.66	9.33	
Large Lymphocytes	.33	3.33	0.00	0.66	
Medium	6.00	4.66	4.66	2.00	
Small	2.66	7.00	15.66	12.66	
Micro	0.33	0.00	00.00	1.00	
Poly-Eosinophiles	1.33	1.33	1.33	1.33	
Monocytes	1.00	0.66	0.00	0.00	
Megacarocytes	0.66	0.66	0.33	0.00	

	5- 9-14	5-16-14	5-23-14	6- 6-14	6-13-14
Poly-Neutrophiles	40.69	52.31	40.66	63.33	39.03
Meta-Myelocytes	27.00	22.00	33.33	6.00	20.33
Neutrophile-Myelocytes.	00.00	00.00	1.66	10.00	6.00
Eosinophile-Myelocytes.	00.00	00.00	0.00	00.00	0.00
Myeloblasts	10.33	6.33	0.00	1.00	4.33
Basophiles	3.33	3.66	5.33	6.00	8.33
Leucoblasts	5.66	7.33	7.70	2.00	3.33
Large Lymphocytes	1.00	0.33	1.00	0.33	3.33
Medium	5.66	4.00	6.00	0.66	4.66
Small	4.00	3.00	2.00	9.33	6.66
Micro	00.00	0.33	0.33	00.00	0.00
Poly-Eosinophiles	1.33	0.00	1.33	1.35	1.00
Monocytes	00.00	0.00	00.00	00.00	0.00
Megacarocytes	1.00	0.00	0.66	0.33	0.00

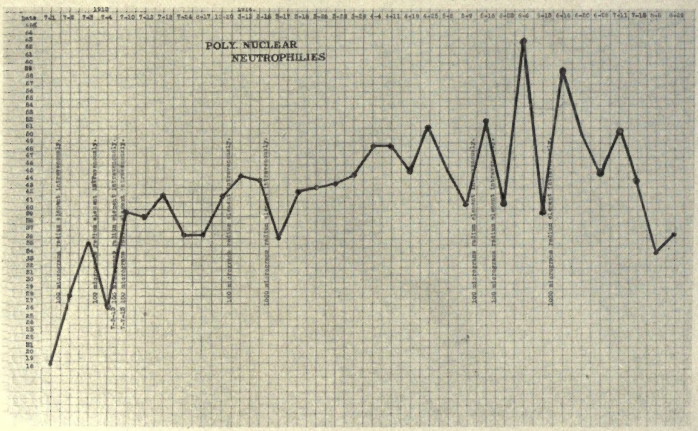
	6-16-14	6-20-14
Poly-Neutrophiles	59.01	50.03
Meta-Myelocytes	5.00	16.33
Neutrophile-Myelocytes.	9.66	00.00
Eosinophile-Myelocytes.	00.00	00.00
Myeloblasts	3.00	7.33
Basophiles	5.00	7.00
Leucoblasts	3.00	8.66
Large Lymphocytes	00.00	0.33
Medium	2.33	1.00
Small	13.00	8.66
Micro	00.00	00.00
Poly-Eosinophiles	00.00	0.66
Monocytes	00.00	00.00
Megacarocytes	00.00	00.00

	6-28-14	7-11-14	7-18-14	8- 8-14	8-29-14
Poly-Neutrophiles	44.00	50.96	44.00	34.00	37.50
Meta-Myelocytes	7.50	9.09	14.00	17.00	16.00
Neutrophile-Myelocytes.		4.54	11.50	8.00	17.00
Eosinophile-Myelocytes.			1.00		0.50
Myeloblasts	4.50	6.36	6.50	9.50	8.00
Basophiles	6.00	6.81	4.50	4.50	2.00
Leucoblasts	9.00	4.54	2.50	10.50	7.00
Large Lymphocytes	0.50		0.50	00.50	3.00
Medium	11.50	2.72	3.00	7.50	6.00
Small	13.00	12.27	11.50	6.00	1.50
Micro		.90			

Poly-Eosinophiles.	63.00	.45	1.00	2.00	1.00
Monocytes.	0.50				
Megacarocytes.	1.50	1.36		0.50	0.50



Case No. 3.—Myelocytes.



Case No. 3—Polynuclear Neutrophiles.

STANDARD CHEMICAL COMPANY

PITTSBURGH, PA.

Reduction Mill of Standard Chemical Co., Canonsburg, Pa.

Miners of Uranium and Vanadium Ores, and Producers of Radium

STANDARD CHEMICAL COMPANY

"STANDARD"

RADIUM PREPARATIONS

"Standard" Radium Solution for Drinking

—

Each bottle contains two micrograms radium element in 60 cc. aqua dist.

—

Maximum-equilibrium constant of radium emanation, 5400 mache units.

"Standard" Radium Solution for Intravenous Use.

—

In Ampulles of 2 cc. N. P. S. S. containing 5, 10, 25, 50, or 100 micrograms radium element.

PERMANENT

PERMANENT

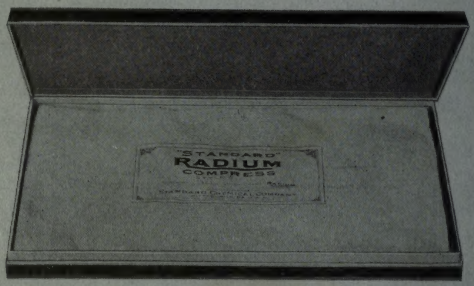
"Standard" Radium Compress

—

A means of applying radium locally for the relief of pain.

—

A flexible pad of standardized, guaranteed radium element content.



PERMANENT RADIO-ACTIVITY

INDICATIONS

Subacute and Chronic Joint and Muscular Conditions.
High Blood Pressure. Nephritis.
The Simple and Pernicious Anemias.

"The value of radium is unquestionably established in chronic and subacute arthritis of all kinds (luetic and tuberculous excepted) acute, subacute and chronic joint and muscular rheumatism (so called) in gout, sciatica, neuralgia, polyneuritis, lumbago and the lancinating pain of tabes."—Rowntree and Baetjer, Journal A. M. A. Oct. 18, 1913.

For Descriptive and Clinical Literature Address

RADIUM CHEMICAL COMPANY

PITTSBURGH

New York
C. Everett Field, M. D.,
50 E. 41st St.

Boston
Samuel Delano, M. D.,
39 Newbury St.

Chicago
C. W. Hanford, M. D.,
749 1st Nat'l Bank Bldg.

San Francisco
Fred I. Lackenbach
Biologic Depot
908 Butler Bldg.